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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/943,072 | 08/30/2001 | David R. Lindsay | LIDR5001JP | 8673 |

29889 7590 10/28/2003

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| EXAMINER | |
|---|---|
| SHEIKH, HUMERA N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | |

DATE MAILED: 10/28/2003

7

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/943,072 | LINDSAY, DAVID R. | |
| | Examiner | Art Unit | |
| | Humera N. Sheikh | 1615 | |

*-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### Status of the Application

Receipt of the Request for Reconsideration filed 08/19/03 is acknowledged.

Claims 1-20 are pending. No amendments have been made. Claims 1-20 remain rejected.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

**Claims 1-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Palermo et al. (US Pat. No. 6,228,863 B1).**

Palermo discloses a controlled release oral dosage pharmaceutical formulation comprising: an analgesically effective amount of an orally active opioid agonist together with an opioid antagonist into an oral dosage form, wherein the amount of antagonist being sufficient to counteract the effects of the opioid agonist/antagonist combination to

provide an aversive effect in a physically dependent human subject when the dosage is orally administered. A method of reducing the abuse potential of an oral dosage form of an opioid analgesic, which comprises combining an analgesically effective amount of an opioid agonist together with an opioid antagonist is also disclosed (see reference column 4, line 36 through column 6, line 35); and claims.

The opioid agonists disclosed are hydrocodone, hydromorphone, oxycodone, morphine sulfate, meperidine, codeine, methadone, or salts thereof, or mixtures thereof (col. 10, lines 8-15); and claims.

Opioid antagonists disclosed include, naltrexone, naloxone, nalmephene, cyclazocine and levallorphan (col. 8, lines 26-35).

Oral administration forms disclosed are tablets, capsules, liquids, powders or granules, microparticles, drops, lozenges, caplets, gelcaps and the like, for example (col. 6, lines 40-45); (col. 12, lines 45-50).

**Claims 1-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Kaiko et al. (US Pat. No. 6,277,384 B1).**

Kaiko discloses a controlled release oral dosage formulation comprising a combination of an orally analgesically effective amount of an opioid agonist and an orally active opioid antagonist in an amount which does not cause a reduction in the level of analgesia elicited from the dosage upon oral administration to a non-therapeutic level and which provides a mildly negative aversive experience in physically dependent

human subjects. A method of preventing oral abuse of an oral opioid formulation by combining an opioid agonist together with an opioid antagonist is also disclosed (see reference column 4, line 46 through column 7, line 42); and claims.

The opioid agonists disclosed are, for example, hydrocodone, hydromorphone, oxymorphone, morphine, meperidine, salts and mixtures of any of the foregoing (col. 11, lines 34-57).

Opioid antagonists include, nalxone, naltrexone, nalmephene, cyclazocine (col. 10, lines 3-12).

Oral administration forms disclosed are tablets, capsules, liquids, powders or granules, microparticles, drops, lozenges, caplets, gelcaps and the like, for example (col. 7, lines 17-42).

***Response to Arguments***

Applicant's arguments filed 08/19/03 have been fully considered but they are not persuasive.

The applicant argued, "The Palermo and Kaiko patents disclose an oral dosage form for reducing abuse of an opioid by incorporating an antagonist into the oral dosage form, which only slightly reduces the effect of the agonist, but not to non-therapeutic levels. In addition, the antagonist of the Palermo and Kaiko patents, in oral dosage form, produces an adverse effect in physically dependent abusers."

These arguments have been fully considered, but were not found to be persuasive. The prior art teaches oral dosage forms comprising combinations of opioid agonists and antagonists and methods of treating pain in human patients in a manner, which minimizes the likelihood of oral abuse of opioid analgesics and also teaches methods of reducing the abuse potential of the oral dosage forms. The applicant's argument that the 'antagonist only slightly reduces the effect of the agonist, but not to non-therapeutic levels' is not persuasive since Palermo teaches such may be the case when, for instance, 'the subjects attempt to take at least twice the usually prescribed dose at a time (and often 2-3 times that dose or more)' (col. 6, lines 18-27). Palermo, also teaches that the preferably, the formulation provides *effective analgesia* when orally administered. "Effective analgesia" is defined as a 'satisfactory reduction in or elimination of pain, along with a tolerable level of side effects, as determined by the human patient (col. 6, lines 50-52). Therefore, the antagonist in the oral formulations of the prior art provide effective reduction effects of the agonist. The argument that the antagonist produces an adverse effect in physically dependent abusers, is also disagreed upon since the art teaches a method of treating pain in humans, which minimizes the likelihood of oral abuse of opioid analgesics.

Next, the applicant argued, "Palermo and Kaiko do not disclose an oral dosage form where the antagonist is not orally active and does not reduce the effect of the agonist when taken orally in a normal fashion. In the present invention, the antagonist is coated with a substance and passes through the body without being absorbed. Only when the coating is broken by crushing beforehand or chewing in the mouth is the

antagonist released and becomes orally active. The Palermo and Kaiko patents disclose an oral dosage that is not encapsulated and is always available to be absorbed. The antagonist claimed by Applicant only becomes orally active when the coating is broken, making the antagonist bioavailable. The method of the present invention, unlike that of the Palermo and Kaiko patents, is not directed to providing an aversive experience for an abuser. "

These arguments have been fully considered, but were not found to be persuasive. The prior art teaches oral dosage forms comprising combinations of opioid agonists and antagonists whereby the dosages are fully effective in the treatment of pain. The applicant's argument that 'only when the coating is broken by crushing beforehand or chewing in the mouth is the antagonist released and becomes orally active' is not persuasive since this is actually a future intended use. A future intended use without structural limitation does not hold patentable weight. The prior art clearly teaches effective reduction of the agonist carried out by the antagonist. Furthermore, the use of a sustained release *coating* of a matrix containing the opioid agonist and opioid antagonist is also taught by the prior art (Palermo, at lines bridging col. 5 & 6). The applicant's argument that the prior art formulations contribute to aversive effects is not persuasive, since it is obvious to one of ordinary skill in this art to include ingredients in an amount and to the extent where they do not adversely affect the patient. Furthermore, the prior art teaches the objective of minimizing the likelihood of oral abuse of opioid analgesics.

In essence, there is no significant distinction observed between the instant invention and the prior art since, both Palermo and Kaiko provide oral opioid agonist/antagonist dosage combinations wherein the antagonist sufficiently counteracts the effects of the agonist and provides effective methods for the alleviation of pain. Hence, the instant invention is rendered obvious and unpatentable over the prior art of record.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**Correspondence**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (703) 308-4429. The examiner can normally be reached on Monday through Friday from 7:00A.M. to 4:30P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

*hns*
October 22, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600